METRONIDAZOLE- metronidazole cream
Fougera Pharmaceuticals Inc.

METRONIDAZOLE
TOPICAL CREAM 0.75%

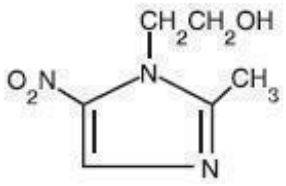
FOR TOPICAL USE ONLY

NOT FOR OPHTHALMIC USE

Rx only

DESCRIPTION

Metronidazole Topical Cream contains metronidazole, USP, at a concentration of 7.5 mg per gram (0.75%) in an emollient cream consisting of emulsifying wax, sorbitol solution, glycerin, isopropyl palmitate, benzyl alcohol, lactic acid, and/or sodium hydroxide to adjust pH, and purified water. Metronidazole is a member of the imidazole class of anti-bacterial agents and is classified therapeutically as an antiprotozoal and antibacterial agent. Chemically, metronidazole is 2-Methyl-5-nitroimidazole-1-ethanol. The molecular formula is $C_6H_9N_3O_3$ and molecular weight is 171.16. Metronidazole is represented by the following structural formula:



CLINICAL PHARMACOLOGY

The mechanisms by which metronidazole acts in the treatment of rosacea are unknown, but appear to include an anti-inflammatory effect.

INDICATIONS AND USAGE

Metronidazole Topical Cream is indicated for topical application in the treatment of inflammatory papules and pustules of rosacea.

CONTRAINDICATIONS

Metronidazole topical cream is contraindicated in individuals with a history of hypersensitivity to metronidazole, or other ingredients of the formulation.

PRECAUTIONS

General: Topical metronidazole has been reported to cause tearing of the eyes. Therefore, contact with the eyes should be avoided. If a reaction suggesting local irritation occurs, patients should be directed to use the medication less frequently or discontinue use. Metronidazole is a nitroimidazole and should be used with care in patients with evidence of, or history of blood dyscrasia.

Information for patients: This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.

Drug interactions: Oral metronidazole has been reported to potentiate the anticoagulant effect of

warfarin and coumarin anticoagulants, resulting in a prolongation of prothrombin time. The effect of topical metronidazole on prothrombin time is not known.

Carcinogenesis, mutagenesis, impairment of fertility: Metronidazole has shown evidence of carcinogenic activity in a number of studies involving chronic, oral administration in mice and rats but not in studies involving hamsters.

Metronidazole has shown evidence of mutagenic activity in several *in vitro* bacterial assay systems. In addition, a dose-response increase in the frequency of micronuclei was observed in mice after intraperitoneal injections and an increase in chromosome aberrations have been reported in patients with Crohn's disease who were treated with 200-1200 mg/day of metronidazole for 1 to 24 months. However, no excess chromosomal aberrations in circulating human lymphocytes have been observed in patients treated for 8 months.

Pregnancy: *Teratogenic effects:* Pregnancy category B

There are no adequate and well-controlled studies with the use of metronidazole topical cream in pregnant women. Metronidazole crosses the placental barrier and enters the fetal circulation rapidly. No fetotoxicity was observed after oral metronidazole in rats or mice. However, because animal reproduction studies are not always predictive of human response and since oral metronidazole has been shown to be a carcinogen in some rodents, this drug should be used during pregnancy only if clearly needed.

Nursing mothers: After oral administration, metronidazole is secreted in breast milk in concentrations similar to those found in the plasma. Even though blood levels are significantly lower with topically applied metronidazole than those achieved after oral administration of metronidazole, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric use: Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

In controlled clinical trials, the total incidence of adverse reactions associated with the use of metronidazole topical cream was approximately 10%. Skin discomfort (burning and stinging) was the most frequently reported event followed by erythema, skin irritation, pruritus and worsening of rosacea. All individual events occurred in less than 3% of patients.

The following additional adverse experiences have been reported with the topical use of metronidazole: dryness, transient redness, metallic taste, tingling or numbness of extremities and nausea.

DOSAGE AND ADMINISTRATION

Apply and rub in a thin layer of metronidazole topical cream twice daily, morning and evening, to entire affected areas after washing.

Areas to be treated should be washed with a mild cleanser before application. Patients may use cosmetics after application of metronidazole topical cream.

HOW SUPPLIED

Metronidazole Topical Cream 0.75% is supplied in a 45 gram tube,

NDC 0168-0323-46

Storage conditions: Store at 20°C to 25°C (68°F to 77°F), excursions permitted 15°C to 30°C

(59°F to 86°F). [See USP Controlled Room Temperature].

E. FOUGERA & CO.
A division of Fougera Pharmaceuticals Inc.
MELVILLE, NEW YORK 11747

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R07/2020
#29

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 45 GRAM TUBE

NDC 0168-0323-46

Fougera®

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TOPICAL CREAM

0.75%

Rx only

FOR TOPICAL USE ONLY
NOT FOR OPHTHALMIC USE

Store at 20°C to 25°C (68°F to 77°F), excursions permitted 15°C to 30°C

(59°F to 86°F). [See USP Controlled Room Temperature].

KEEP OUT OF THE REACH OF CHILDREN.

NET WT 45 grams

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 45 GRAM CARTON

NDC 0168-0323-46

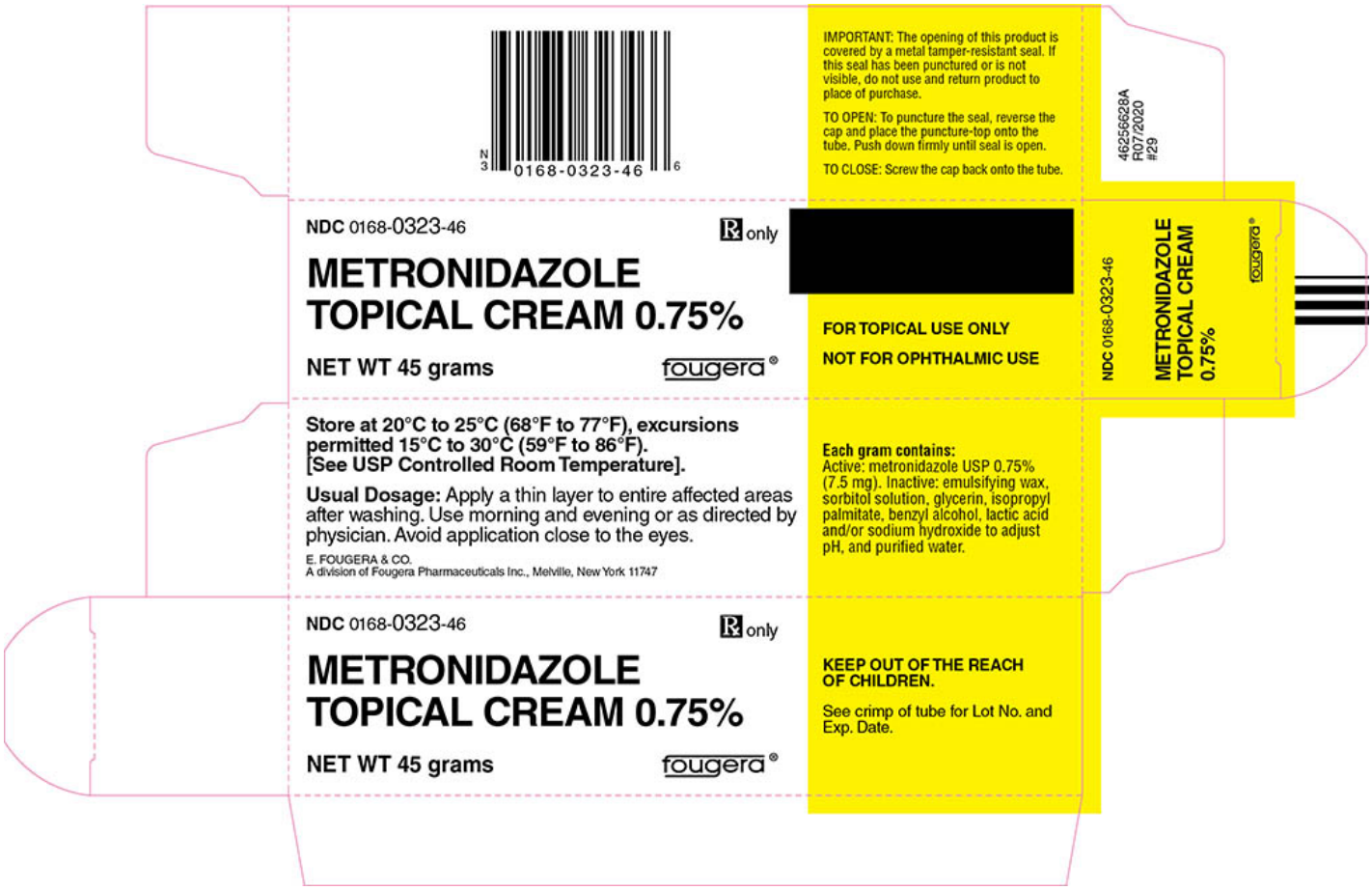
Rx only

Fougera®

METRONIDAZOLE
TOPICAL CREAM 0.75%

FOR TOPICAL USE ONLY
NOT FOR OPHTHALMIC USE

NET WT 45 grams



METRONIDAZOLE

metronidazole cream

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0168-0323
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
metronidazole (UNII: 140QMO216E) (metronidazole - UNII:140QMO216E)	metronidazole	7.5 mg in 1 g

Inactive Ingredients	
Ingredient Name	**Strength**
sorbitol (UNII: 506T60A25R)	
glycerin (UNII: PDC6A3C0OX)	
isopropyl palmitate (UNII: 8CRQ2TH63M)	
benzyl alcohol (UNII: LKG8494WBH)	
LACTIC ACID, UNSPECIFIED FORM (UNII: 33X04XA5AT)	
sodium hydroxide (UNII: 55X04QC32I)	
water (UNII: 059QF0KO0R)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0168-0323-46	45 g in 1 TUBE; Type 0: Not a Combination Product	05/28/2004	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA076408	05/28/2004	

Labeler - Fougera Pharmaceuticals Inc. (043838424)

Revised: 8/2020 Fougera Pharmaceuticals Inc.